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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,503	12/13/2005	Hidekazu Inoue	69681.000006	4612

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HUNTON & WILLIAMS LLP
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER	
MURRAY, JEFFREY H	

ART UNIT	PAPER NUMBER
1624	

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10/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,503	INOUE ET AL.	
	Examiner	Art Unit	
	Jeffrey H. Murray	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/13/2005 & 03/06/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. This action is in response to a restriction requirement election filed on October 5, 2007. The applicants have elected Group IV with traverse but have given no arguments. Therefore the restriction is proper and deemed FINAL. Applicants were correct in pointing out a typographical error in regards to A being CR^4, not CH, and A will be treated as such throughout the search. There are eleven claims pending and ten claims under consideration. Claim 3 has been withdrawn from consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. This is the first action on the merits. The present invention relates to imidazotriazinone compounds, pharmaceutically acceptable salts and solvates thereof, having PDE 7 (phosphodiesterase VII) inhibiting effect. These compounds are effective compounds for treating various kinds of disease such as allergic disease, inflammatory disease and immunologic disease.

After conducting a further search, it is determined that the restriction will be reduced to simply two groups: Groups I-IV will be reduced to a single group containing compounds of Formula IA while Groups V-VIII will be reduced to a single group containing compounds of Formula IB.

Priority

2. Acknowledgment is made of Applicant's claim for foreign priority. This application is U.S. Application No. 10/560,503, filed December 13, 2005, and is a

national stage entry of PCT application PCT/JP04/08642, filed June 11, 2004 which claims foreign priority to Japanese Application No. 2003-170095, filed June 12, 2003.

Specification

3. The use of the trademarks POLYTRON and SEPHADEX has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

Claim Objections

5. Claim 3 is objected to because of the following informalities: Claim 3 is a non-elected claim and should be withdrawn from the application. Appropriate correction is required.

6. Claim 6 is objected to because of the following informalities: Claim 6 states, "in which A is CR^4." Due to the restriction election, this portion of the claim is unnecessary. Appropriate correction is required.

7. Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Due to the restriction election, Claim 7 already has "B is CH". Therefore claim 7 is not further limiting.

Claim Rejections - 35 USC § 112, 1st

8. Claims 1, 2 and 4-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound, composition or pharmaceutically acceptable salt, does not reasonably provide enablement for a solvate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics* Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1) *Amount of guidance provided by Applicant.* Applicant has provided no guidance, examples, or provided data and/or testing results of any solvates in the current application.

2) Unpredictability in the art. Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent; these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates. (*Advanced Drug Delivery Reviews*; **48**, (2001) 3-26.

3) *Number of working examples.* Applicant has provided no working examples of a solvate in the present application.

4) *Nature of the invention.* The nature of this invention relates to imidazotriazinone compounds, pharmaceutically acceptable salts and solvates thereof, having PDE 7 (phosphodiesterase VII) inhibiting effect. These compounds are effective compounds for treating various kinds of disease such as allergic disease, inflammatory disease and immunologic disease.

5) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a Ph.D. degree, and having several years of bench experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making these compounds or compositions.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

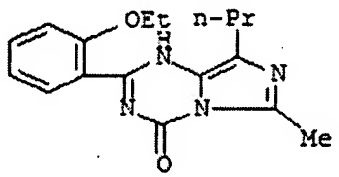
9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

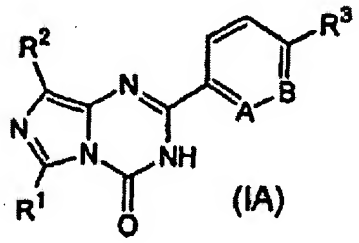
10. Claims 1, 2, and 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niewoehner et. al. (WO 2001047928) in view of In re Hass et

al. (CCPA 1944) 141F2d 122 and 127, 60 USPQ 544 and 548; and In re Henze (CCPA 1950) 181 F2d 198, 85 USPQ 261. The current application recites a variety of specific novel substituted imidazotriazinone compounds and compositions that can be used as phosphodiesterase VII inhibitors. These compounds all contain a imidazotriazinone core with various substitutents.

Niewoehner et. al., teaches a compound which is similar in scope to the current application. Within Niewoehner et. al., the same core structure is present with one difference. The core of Niewoehner et. al. is a substituted imidazotriazinone containing a as seen below:



where R^1 is a *n*-propyl group. This differs only slightly with the current application and the elected Formula IA which has the following structure:



where A is CR^4 and B is CH. In particular, R^1 can contain a substituted or unsubstituted cycloalkyl group or a *t*-butyl group. Therefore, R^1 between the two compounds differs only by one atom and two hydrogen atoms.

The CCPA has defined a homologous series as a family of chemically related compounds, the composition of which varies from member to member by a CH2 (one atom of carbon and two hydrogen). In re Coes, Jr. (CCPA 1949) 173 F2d 1012, 81 USPQ 369. The Court of Appeals for the District of Columbia applied a broader definition and defined a homolog (homologue) as a member of a series of compounds in which each member differs from the next member by a constant number of atoms. Carr. Pats.v. Deutsche Gold-und-Sllber, etc. (CADC 1968) 397 F2d 656,157 USPQ 549.

The "Hass-Henze Doctrine" evolved from three CCPA cases, viz., *In re Hass et al.* (CCPA 1944) 141 F2d 122 and 127, 60 USPQ 544 and 548; and *In re Henze* (CCPA 1950) 181 F2d 198, 85 USPQ 261. In the *Henze* decision, the Court said:

> "The nature of homologues and the close relationship the physical and chemical properties of one member of a series bears to adjacent members is such that a presumption of unpatentability arises against a claim directed to a composition of matter, the adjacent homologue of which is old in the art. The burden is on the applicant to rebut that presumption by a showing that the claimed compound possesses unobvious or unexpected beneficial properties not actually possessed by the prior art homologue. It is immaterial that the prior art homologue may not be recognized or known to be useful for the same purpose or to possess the same properties as the claimed compound. The CCPA concluded that because the characteristics normally possessed by members of a homologous series are principally the same, varying gradually from member to member, chemists knowing the properties of one member of a series would in general know what to expect in adjacent members so that a mere difference in degree is not the marked superiority which will ordinarily remove the unpatentability of adjacent homologues of old substances. Contra, where no use for the prior art compound is known. *In m Stemniski* (CCPA 1971) 444 F2d 581, 170 USPQ 343, and cases cited therein. Whether a

> compound is patentable over a prior art homologue or isomer is a question to be decided in each case. *In re Hass et* al., *supra."*

The 'Hass-Henze Doctrine" stands for the proposition that, "If that which appears at first blush to be obvious though new is shown by evidence not to be obvious then the evidence prevails over surmise or unsupported contention and rejection based on obviousness must fail." In re *Papesch* (CCPA 1963) 315 F2d 381, 137 USPQ 43, 48. The presumption that homologues are unpatentably obvious is an inference of fact, viz., that adjacent homologs are expected to have similar properties which places a 'burden of persuasion' on the applicant who asserted a contrary fact. In *re Mills* (CCPA 1960) 281 F2d 218, 126 USPQ 513.

The test of patentability of a compound that is a homologue of a prior art compound is whether the claimed compound possesses beneficial characteristics which are unexpected and unobvious. *Sterling Drug, Inc. v. Watson, Comr. Pals.* (DCDC 1955) 135 FSupp 173, 108 USPQ 37. The properties must be clearly outside of the expectations which knowledge of his science would inform the trained chemist or the biologists, pharmacologists, medical clinicians or other competent trained personnel who carry out the testing in the field, should be inherent in the claimed product. *Ruskin v. Watson, Cow. Pats.* (DCDC 1954) 123 FSupp 33, 101 USPQ 275.

Relating the information from In re Hass et al. (CCPA 1944) 141F2d 122 and 127, 60 USPQ 544 and 548; and In re Henze (CCPA 1950) 181 F2d 198, 85 USPQ 261 to Niewoehner et. al. publication, it would have been obvious for a

person of ordinary skill in the art to try replacing the *n*-propyl group with a *t*-butyl group in the same position.

The claims above are obvious because the substitution of one known element for another (*t*-butyl for *n*-propyl) would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Double Patenting

11. Applicant is advised that should claim 10 be found allowable, claim 11 will be objected to respectively under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

6. Claims 1,2 and 4-11 are rejected.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is (571) 272-9023. The examiner can normally be reached on Mon-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, James O. Wilson can be reached at 571-272-9023. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a US PTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JHM

James O. Wilson
Supervisory Patent Examiner
Art Unit 1624